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Changes of lead levels in 24-h urine from 1985 to 1998 in Japanese adults

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Abstract

To determine whether current environmental lead (Pb) levels are causing any progressive changes in urinary Pb levels, 24-h urine samples were collected from 277 subjects (159 men and 118 women) in 1985, 312 subjects (155 men and 157 women) in 1993, and 311 subjects (156 men and 155 women) in 1998. All of the subjects worked in the same factory. The urinary Pb concentration was analyzed by flameless atomic absorption spectrophotometry. The geometric means for men were 4.74, 2.67 and 1.31 μg/day; 3.17, 1.78 and 1.04 μg/g creatinine; and 3.18, 1.99 and 0.98 μg/l urine in 1985, 1993 and 1998, respectively. The values for women were 3.22, 2.14 and 0.97 μg/day; 3.35, 2.26 and 1.15 μg/g creatinine; and 2.49, 1.86 and 0.83 μg/l urine, respectively. These results demonstrated that Pb levels in 24-h urine decreased significantly in the 13-year period ($P < 0.01$).

Keywords: Background lead levels; Lead levels in 24-h urine; Adult population in Japan; Biological monitoring of lead

1. Introduction

Human civilization and a concomitant increase in industrial activity have gradually redistributed many toxic metals from the earth's crust to the environment, thereby increasing the possibility of human exposure. These metals serve no biological function and are toxic even at low doses. Among these metals, lead (Pb) is especially widespread in our environment due to its common industrial and domestic use, e.g. anti-knocking agent in gasoline and house paints. Because of the risk of Pb for the general population, especially fetuses and children, it is necessary to regularly monitor the environmental exposure to Pb in the general population (Chowdhury and Chandra, 1987; Baghurst et al., 1992; Staessen et al., 1994; Muldoon et al., 1996; Spevackova et al., 1997).

Pb is a multiple-source pollutant. Therefore, biological monitoring is the best source of information on total Pb exposure. In a previous paper we reported that Pb levels in 24-h urine (μg/day) taken in 1993 were significantly lower than those

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in 1985 (Jin et al., 1997). To determine whether the decreasing trend of Pb levels in 24-h urine in Japan is being maintained we examined the Pb levels in 24-h urine from the same place and used the same method in 1998 as we did in 1985 and 1993, and determined the new Pb background levels in 24-h urine by sex in Japan. As few investigators have attempted this demanding type of sampling, the data presented in this paper may add information to this subject.

On the other hand it is well known that Pb levels in spot urine can be influenced by many factors, including fluid intake and fluctuation in the specific gravity of urine. Pb level in spot urine is not a reliable indicator of Pb exposure, particularly if a precise evaluation is required (Friberg et al., 1986; Watanabe et al., 1987). To determine whether the Pb level in 24-h urine shows a significant difference according to different sampling times, we collected the 24-h urine samples twice from the same subject within a 1-month period in 1998.

2. Materials and methods

2.1. Subjects and sampling

The 24-h urine samples were collected three times during the 13-year period study, in 1985, 1993, and 1998, from workers in the same factory in the Toyama prefecture, Japan. In this factory aluminum alloys were used to produce zippers and window frames, etc., and so there was no known occupational Pb pollution. The employees of this factory numbered more than 10 000. The age range was 20–59 years. Approximately 300 subjects were randomly sampled each time on the basis of statistical techniques, as far as possible equally distributed in men and women, and in every age group.

A total of 278 subjects (159 men and 119 women) in 1985, 321 subjects (161 men and 160 women) in 1993, and 312 subjects (157 men and 155 women) in 1998 were examined. The age range was 20–59 years in 1985 and 1993, and 40–59 years in 1998. A 24-h urine sample was collected in a metal-free, wide neck polyethylene container. The containers used for sampling the urine were used both at home and the office. None of the subjects lived far from the factory, and so no urine was lost while commuting. The examinees were carefully instructed to keep these containers closed in order to prevent metal contamination. In 1998 the 24-h urine of every subject was collected twice within a 1-month period.

2.2. Urinalysis for Pb

The collected 24-h urine was well mixed and divided into several metal free polyethylene test tubes. One of these test tubes with 10 ml urine for Pb analysis was acidified by adding 0.1 ml concentrated nitric acid in order to prevent Pb precipitation, then was stored in a -20°C freezer until the analysis. Urinary Pb concentrations were determined by flameless atomic absorption spectrophotometry after wet digestion followed by solvent extraction, a conventional method used to determine Pb levels in the urine of normal populations. The validity of this method has already been established (Honda et al., 1989; Jin et al., 1997).

The sensitivity limit for Pb determination was 0.1 ppb of urine, and therefore results below this level were reported as 0.1 ppb. In order to confirm whether the samples analyzed at different times could be compared, 50 urinary specimens drawn from the samples taken in 1985, in which the Pb concentrations varied from low to high, were determined while the samples taken in 1993 were being determined. The correlation coefficient between the two determinations was 0.96 and the regression slope was 1.06. Of these 50 urinary specimens 15 were measured again while the samples taken in 1998 were being determined. The correlation coefficient between the results obtained in 1993 and 1998 was 0.97, and the regression slope was 1.11.

Urinary creatinine concentration was determined by the Jaffe reaction method (Bonsnes and Taussky, 1945).

2.3. Reagents and laboratory wares

Acids (a specific grade for pollutant metal analysis) were purchased from Wako Pure Chemical

Industries (Osaka, Japan). All glass and plastic wares were washed with detergent and acid, and rinsed with redistilled water avoid metal leaching. Ammonium nitrate solution (4 M) was purified before use by adding APDC-MIBK to remove the Pb.

2.4. Statistical analysis

Statistical analysis was conducted using SAS software. In these procedures, three units were used to express Pb levels in 24-h urine, i.e. μg/day, μg/g creatinine (g cr.), and μg/l urine. Distributions of all biological indicators were normalized by log-transformation. Paired sample t-test was used to evaluate the paired data in 1998. Pearson's correlation coefficient was used to evaluate bivariate correlationships. Significance of the difference in age or time was evaluated by analysis of variance (ANOVA), and post-hoc comparison was evaluated by Student–Newman–Keuls test. Significance of the difference between sexes was evaluated by Student's t-test. Significance levels of these statistical analyses were derived from the two-tailed test. A significance level of 0.05 for the hypothesis test was used.

3. Results

3.1. Analysis on paired samples taken in 1998

Urine volume, creatinine levels and Pb levels in 24-h urine between the paired samples are summarized by sex in Table 1. Except for the levels of creatinine in men, the differences in the mean levels of these indicators between the paired samples were not significant. The correlation of these indicators between the paired samples were all significant ($P < 0.01$).

3.2. Pb levels in 24-h urine according to sex and age

Pb levels in 24-h urine expressed as μg/day, μg/g cr., and μg/l urine subdivided according to sex and age group are shown in Tables 2–4. For Pb levels in 24-h urine (μg/day), except for those in the 30–39 and 50–59 age groups in 1993 and the 40–49 age group in 1998, Pb levels in the other age groups and in all total-cases were significantly higher in men than in women (Table 2). For Pb levels in 24-urine (μg/g cr.), except for

Table 1
Comparison and correlation between paired-sampling samples[a]

Age range	Cases	The first time		The second time		P (t-test)	R	P (corr)
		GM	GSD	GM	GSD			
Male								
Vol (l/day)	147	1.386	1.397	1.440	1.350	NS	0.5001	<0.01
Cr (g/day)	147	1.052	0.366	0.987	0.333	<0.05	0.5259	<0.01
Pb levels								
μg/day	147	1.37	1.84	1.28	1.99	NS	0.5228	<0.01
μg/g cr.	147	0.99	1.81	0.96	2.03	NS	0.5211	<0.01
μg/l	147	0.99	1.88	0.89	2.08	NS	0.5704	<0.01
Female								
Vol (l/day)	148	1.237	1.368	1.262	1.391	NS	0.5057	<0.01
Cr (g/day)	148	0.740	0.250	0.758	0.235	NS	0.4294	<0.01
Pb levels								
μg/day	148	0.98	2.03	0.99	2.03	NS	0.5393	<0.01
μg/g cr.	148	1.13	2.07	1.08	2.01	NS	0.5263	<0.01
μg/l	148	0.79	2.03	0.78	2.00	NS	0.3852	<0.01

[a] GM, geometric mean; GSD, geometric S.D., P(t-test), comparison of means between paired samples evaluated by paired-sample t-test; R, Pearson's correlation coefficient; P(corr), correlation between paired samples evaluated by Pearson's correlation coefficient; NS, not significant.

those in the 50–59 age group and total-cases in 1993 and in the 40–49 age groups in 1998, Pb levels in the other age groups and total-cases were not significantly different (Table 3). For Pb levels in 24-h urine (μg/l urine), significant gender differences were seen in 1985 and 1998, but no significant gender difference was seen in 1993 except for the 40–49 age group (Table 4).

As for Pb levels in 24-h urine (μg/day and μg/g cr.), according to age, no significant differences in Pb levels in the different age groups were observed in 1985 or 1993, except for the female group in 1985 (Tables 2 and 3). Pb levels in 24-h urine (μg/l urine) showed significant differences only in men in 1985 and in 1993 (Table 4).

3.3. Comparison of the findings in 1985, 1993 and 1998

Pb levels in 24-h urine in age-matched groups and total-cases in men and women were compared for the 1985, 1993 and 1998 findings. In 1998 the average of the paired urine of every subject was used to represent the findings. Pb levels in 24-h urine (μg/day) were significantly lower in 1998 than 1993 and lower in 1993 than 1985 in all age groups in both sexes, except for the difference between women aged 20–29 in 1985 and 1993. There was an apparent downward trend of Pb levels with time within the period from 1985 to 1998 (Table 2). Pb levels in 24-h urine (μg/g cr. and μg/l urine) also showed a downward trend with time (Tables 3 and 4).

4. Discussion

In our previous study we reported Pb levels in 24-h urine expressed as μg/day. As most studies on urinary Pb levels have used spot urine, the Pb levels in 24-h urine were also given in terms of Pb levels μg/g cr. and μg/l urine (non-adjusted) in the present paper.

In the previous study we found that Pb levels in 24-h urine were significantly lower in 1993 than 1985 in both sexes, and those values were significantly higher in men than in women. We also found that Pb levels in 24-h urine have no relationship to age or smoking habits. Those results were obtained from 24-h urine taken one time. In the present study we collected 24-h urine twice from every subject in 1998 to investigate whether the paired samples show the same Pb levels in both sexes. As Pb levels in 24-h urine had no relationship to age in our previous study, and collection of 24-h urine is cumbersome, we collected 24-h urine only from the subjects aged 40–59 years in 1998. Until now few reports have relied on this demanding type of sampling. Analysis on paired samples suggested that Pb levels in 24-h urine expressed as μg/day, μg/g cr. and μg/l urine were stable not only on a group basis but also at a personal level. It proved that Pb levels in 24-h urine did not fluctuate among different sampling times within a short period of time, and were a reliable indicator for Pb biological monitoring.

The results of the previous paper suggested that there were no age-related changes in Pb levels in 24-h urine (μg/day) in either sex from 20 to 59 years of age. In the present study we also compared Pb levels in 24-h urine samples according to age in the concentrations expressed as μg/g cr. and μg/l urine. The results indicated that Pb levels expressed in these units were not strongly influenced by age differences. Differences of geometric mean values according to age groups were rather small although statistical analysis showed the existence of significant differences in some age groups.

The relationship between blood Pb levels and age is not clear in the literature. Most studies suggested that blood Pb levels did not related to age in the adult population (Elinder et al., 1983; Watanabe et al., 1985; Friberg et al. 1986; James et al., 1994; Yang et al., 1996; Weyermann and Brenner, 1997), although some studies reported that blood Pb levels increased with age (Pallotti et al., 1983; Staessen et al., 1990; Berode et al., 1991; Sokas et al., 1997). Blood Pb level may be the indicator of environmental Pb exposure and Pb burden in the soft tissue. On the other hand, the urinary Pb level may be related to the Pb burden not only in soft tissue but also in the bone. Although Pb levels in the bone increase throughout life the biological half time of Pb in the bone

Table 2
Comparison of lead levels in 24-h urine among samples taken in 1985, 1993 and 1998, age groups and between sexes[a]

Age range	Urinary lead levels (μg/day)												*P* (S1/S2/S3)
	Samples taken in 1985				Samples taken in 1993				Samples taken in 1998				
	N	GM	GSD	*P* (M/F)	*N*	GM	GSD	*P* (M/F)	*N*	GM	GSD	*P* (M/F)	
Male													
20–29	39	4.65	1.56	<0.01	39	2.84	1.80	<0.05					<0.01
30–39	40	4.93	1.35	<0.01	38	2.66	2.01	NS					<0.01
40–49	40	4.71	1.50a	<0.01	39	3.04	1.77b	<0.01	75	1.11	1.74c	NS	<0.01
50–59	40	4.65	1.42a	<0.01	39	2.20	2.26b	NS	81	1.67	1.55c	<0.01	<0.01
Total	159	4.74	1.46a	<0.01	155	2.67	1.98b	<0.01	156	1.37	1.71c	<0.01	<0.01
P (age)		NS				NS				P<0.01			
Female													
20–29	29	2.75a	1.37		39	2.04	2.20						NS
30–39	29	3.21ab	1.39		35	2.34	2.15						<0.05
40–49	30	3.53b	1.47a		44	1.90	2.11b		78	0.96	1.72c		<0.01
50–59	30	3.41b	1.41a		39	2.37	1.74b		77	1.08	1.95c		<0.01
Total	118	3.21	1.42a		157	2.14	2.05b		155	1.02	1.84c		<0.01
P (age)		<0.05				NS				NS			

[a] Results of variance analysis: *P* (M/F), comparison between males and females in the same population; *P* (S1/S2/S3), comparison among findings in 1985, 1993 and 1998; GM with the same letter are not significantly different; GSD with the same letter are not significantly different; *P* (age), comparison among age groups; NS, not significant.

Table 3
Comparison of lead levels per gram creatinine among samples taken in 1985, 1993 and 1998, age groups and between sexes[a]

Age range	Urinary lead levels (μg/g cr.)												*P* (S1/S2/S3)
	Samples taken in 1985				Samples taken in 1993				Samples taken in 1998				
	N	GM	GSD	*P* (M/F)	*N*	GM	GSD	*P* (M/F)	*N*	GM	GSD	*P* (M/F)	
Male													
20–29	39	2.89	1.62	NS	39	1.73	1.79	NS					<0.01
30–39	40	3.06	1.35	NS	38	1.70	2.09	NS					<0.01
40–49	40	3.30	1.42a	NS	39	2.15	1.77b	NS	75	0.82	1.89c	<0.05	<0.01
50–59	40	3.47	1.36a	NS	39	1.58	2.28b	<0.01	81	1.29	1.53b	NS	<0.01
Total	159	3.17	1.45a	NS	155	1.78	1.99b	<0.01	156	1.04	1.79c	NS	<0.01
P (age)		NS				NS				P<0.01			
Female													
20–29	29	2.68a	1.41		39	2.07	2.23						NS
30–39	29	3.22b	1.31		35	2.31	2.19						<0.05
40–49	30	3.72b	1.46a		44	1.94	2.11b		78	1.03	1.73c		<0.01
50–59	30	3.92b	1.38a		39	2.90	1.67b		77	1.29	1.94c		<0.01
Total	118	3.35	1.43a		157	2.26	2.07b		155	1.15	1.85c		<0.01
P (age)		<0.01				NS				<0.05			

[a] Results of variance analysis: *P* (M/F), comparison between males and females in the same population; *P* (S1/S2/S3), comparison among findings in 1985, 1993 and 1998; GM with the same letter are not significantly different; GSD with the same letter are not significantly different; *P* (age), comparison among age groups; NS, not significant.

Table 4
Comparison of lead levels per liter urine (non-adjusted) among samples taken in 1985, 1993 and 1998, age groups and between sexes[a]

Age range	Urinary lead levels (μg/l)												*P* (S1/S2/S3)
	Samples taken in 1985				Samples taken in 1993				Samples taken in 1998				
	N	GM	GSD	*P* (M/F)	*N*	GM	GSD	*P* (M/F)	*N*	GM	GSD	*P* (M/F)	
Male													
20–29	39	3.51a	1.41	<0.01	39	2.51a	1.75	NS					<0.01
30–39	40	3.30ab	1.32	<0.01	38	1.74ab	1.90	NS					<0.01
40–49	40	3.03ab	1.36a	<0.01	39	2.28a	1.84b	<0.01	75	0.81	1.85c	NS	<0.01
50–59	40	2.90b	2.90a	<0.01	39	1.56b	2.49b	NS	81	1.17	1.53c	<0.01	<0.01
Total	159	3.18	1.37a	<0.01	155	1.99	2.04b	NS	156	0.98	1.74c	<0.05	<0.01
P (age)		<0.05				<0.01				<0.01			
Female													
20–29	29	2.70	1.24		39	2.23	2.25						NS
30–39	29	2.53	1.36		35	2.06	2.31						NS
40–49	30	2.45	1.39a		44	1.46	2.21b		78	0.81	1.77c		<0.01
50–59	30	2.32	1.30a		39	1.87	1.85a		77	0.85	1.78b		<0.01
Total	118	2.49	1.33a		157	1.86	2.18b		155	0.83	1.77c		<0.01
P (age)		NS				NS				NS			

[a] Results of variance analysis: *P* (M/F), comparison between males and females in the same population; *P* (S1/S2/S3), comparison among findings in 1985, 1993 and 1998; GM with the same letter are not significantly different; GSD with the same letter are not significantly different; *P* (age), comparison among age groups; NS, not significant.

is very long, about 20 years (the value in soft tissue is about 20 days) (Friberg et al., 1986). It is considered that the Pb burden in the bone may have a weak influence on the urinary Pb level. Watanabe et al. (1987) investigated Pb concentrations in the spot urine of farmers in the non-polluted area of Japan and reported that urinary Pb levels did not increase with age.

As for the gender difference of Pb levels in 24-h urine, there were clear differences in the urinary levels expressed as μg/day and μg/l urine in 1985. Pb levels were significantly higher in men than in women. However, a significant difference was not found in the concentration expressed as μg/g cr. in 1985. In the urinary samples taken in 1993 and 1998 some age groups showed a significant difference between men and women, but the others did not in the urinary levels expressed as μg/day, μg/g cr. and μg/l urine. It seems that Pb levels in 24-h urine expressed as μg/day and μg/l urine were higher in men than in women. It should be noted that as the Pb levels in 24-h urine decreased with time continually in both men and women, the difference of Pb levels in 24-h urine expressed as μg/day and μg/l urine between men and women became smaller and smaller than before. On the other hand, Pb levels expressed as μg/g cr. were almost equal between men and women. These results are in accordance with the conclusion reported by Staessen et al. (1984). It suggested that when Pb levels in urine were adjusted for creatinine, because of the obvious difference in urinary creatinine concentrations between the sexes, the data could not show the Pb burden accurately between men and women.

During the past 20 years legal restrictions on industry emissions and reduction of Pb in petrol have led to major reductions of environmental Pb contamination in many industrialized countries. Consequently, the population of these countries has enjoyed a decrease in Pb burden (Quinn and Delves, 1989; Ducoffre et al., 1990; Probst-Hensch et al., 1993; James et al., 1994; Wietlisbach et al., 1995). The median Pb levels in blood in the general population decreased from the 1970s to the 1980s in these industrial countries, and blood Pb levels appeared to decrease to a lesser extent in the 1990s (Friberg et al., 1986; Ducoffre et al. 1990; Probst-Hensch et al., 1993). In Japan, as Pb-free gasoline has been supplied since the 1970s, environmental Pb pollution decreased continually. Pb concentration in the air in Tokyo have decreased from 0.67 $\mu g/m^3$ in 1970 to 0.50 $\mu g/m^3$ in 1975 and 0.26$\mu g/m^3$ in 1976 to less than 0.10 $\mu g/m^3$ in recent times. The Pb levels in urine in Japanese male adults have decreased from about 20 μg/l urine (adjusted by specific gravity, arithmetic mean) in the 1970s to about 10 μg/l urine in the early 1980s and to less than 5 μg/l urine in the late 1980s (Horiguchi, 1993). However, there are few studies on the changes in urinary Pb levels in the 1990s as compared with those in the 1980s. In the present study, we compared the Pb levels in 24-h urine of adult population in 1985, 1993 and 1998. As all of these data were determined in the same laboratory using the same method, and the accuracy of analysis was controlled continually, the present results may be more useful for comparing the urinary Pb levels and Pb environmental exposure between the 1990s and the 1980s in Japan. Our findings suggested that environmental Pb exposure was lower in the 1990s than in the 1980s and continually decreased during the 1990s in Japan. It should be noted that the downward trend was observed in all urinary levels expressed as μg/day, μg/g cr. and μg/l urine.

On the basis of the present study it may be concluded that Pb levels in 24-h urine have shown a downward trend over the last 13 years in Japan and can be used as a reliable indicator of biological monitoring.

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